Progestin-Only Contraception

PROGESTIN-ONLY CONTRACEPTIVE methods work by altering the cervical mucus, making it thick and scanty so that it is more difficult for sperm to penetrate; by affecting motility of the oviduct and uterus, thus affecting ova and sperm transport; and by altering the endometrium so that less glycogen is available for blastocyst survival. Ovulation may be inhibited as infrequently as 10% of the time. The progestin-only pill, used in England for years, has a failure rate of 1% to 2.5%. Although intermittent irregular bleeding is a frequent side effect, the progestin-only pill is especially useful for a woman who is breastfeeding or who has estrogen-related side effects, such as chloasma, using the combined pill. Injectable progesterone is used worldwide, but its use has not been approved in the United States, primarily because mammary tumors developed in beagle dogs during experimental testing; this work is being repeated. Vaginal rings and intrauterine devices that release progesterone have also been developed.

Recently approved by the Food and Drug Administration is the levonorgestrel implant, Norplant, which releases 50 to 80 μg of levonorgestrel daily in the first year, then 30 to 35 μg in subsequent years. With this progestin-only method, ovulation is inhibited in at least 50% of cycles. Using a trochar, six matchstick-size silastic capsules are placed under the skin of the upper inner arm. It is effective for five years and has a 98.5% effectiveness rate. Side effects include irregular menstrual bleeding (60% to 70%) and headaches (5% to 20%). Placement takes about 15 minutes and is easier than removal because over time, fat and fibrous tissue can develop around the capsules. A new system, Norplant-2, is being developed that would use only two capsules, provide the same efficacy, last for three years, and, because of requiring fewer capsules, be easier to insert and remove. It is likely that Norplant will soon be replaced by Norplant-2.

Next on the horizon is a biodegradable progestin-only implant. One form will be norethindrone in cholesterol. It is not clear how easy these will be to remove in a patient with severe bleeding or if a patient requests removal. In fact, recent data indicate that it will not be possible to remove them.

There are several questions and concerns with the progestin-only methods. One is the common side effect of irregular bleeding, which leads 12% to 19% of women to discontinue the levonorgestrel implant. Levonorgestrel is one of the more androgenic progestins currently marketed in the United States, and, although the capsules release a low dose, the potential may exist for side effects such as those seen with androgenic progestins in the oral contraceptive pill, for instance, acne, hirsutism, and depression. Clinical trials have shown an incidence of acne of 5% to 20% and have not reported the other side effects. Although initial trials of the levonorgestrel implant have demonstrated a drop of 5% to 15% of both high-density lipoprotein (HDL) and low-density lipoprotein (LDL) levels, longer term studies of its effect on lipids will be necessary because it is known that the progestin component of the combined pill tends to increase LDL levels and decrease HDL levels. Finally, recent studies in macaque monkeys show that progestin-only contraception was more likely to cause atherosclerosis than balanced estrogen-progestin contraception.

On the one hand, the levonorgestrel implant will be a useful method for women who find it difficult to comply with other contraceptive options and who want an effective method. On the other hand, side effects may lead many women to have them removed.

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Pregnancy Testing—Home and Office

THE RAPIDLY CHANGING TECHNOLOGY for pregnancy tests has greatly enhanced our ability to confirm early pregnancy not only in the office or laboratory setting but also in the home. Home pregnancy tests were first marketed in the 1970s, and they have been increasingly accepted (used by about 30% of pregnant women) despite concern regarding their accuracy. The first home pregnancy test, "ept," did not require Food and Drug Administration (FDA) approval. The FDA has judged all subsequent products to be "substantially equivalent," thus free from regulation. While manufacturers claim 98% to 99% accuracy as early as six days after the missed menses, one study resulted in a positive predictive value of only 65.5% for pregnancies of nine days or less from the missed menses.

Until recently, most office pregnancy tests were latex agglutination inhibition tests or hemagglutination inhibition tests (performed using either slide or tube techniques). These have generally been replaced by monoclonal antibody tests, which are more sensitive and specific. Latex agglutination inhibition slide tests are positive with human chorionic gonadotropin (hCG) levels of 1,500 to 3,500 IU per liter 38 to 42 days after the last menstrual period. Latex agglutination and hemagglutination inhibition tube tests are slightly more sensitive, turning positive with hCG levels of 750 to 850 IU per liter 35 days after the last menstrual period.

Monoclonal antibody tests are far more sensitive, turning positive with hCG levels of 20 to 50 IU per liter 24 to 27 days after the last menstrual period. Urine is placed on a membrane with anti-α monoclonal antibodies; hCG in the urine binds to the membrane. A solution is added that reacts with the β-subunit, creating an antibody-hCG-antibody complex. This second antibody attaches to the complex, creating a blue dot, which indicates a positive test. While monoclonal antibody tests are usually done using urine, they are also available using serum (accurate even with hCG concentrations as low as 10 IU per liter). An extra step is required to achieve this small increase in sensitivity, which is seldom of clinical relevance compared with urine tests.

The percentage of positive tests at 13 days and 16 days after ovulation (documented by ultrasonography) or follicular aspiration is 75% and 100%, respectively, for "FACT," 60% and 75% for "Daisy 2," and 95% and 95% for "Advance." FACT and Daisy 2 use monoclonal antibodies that detect hCG in urine with a hemagglutination inhibition assay. Advance uses monoclonal antibodies that assist enzymes specifically to detect hCG.

The reliability of any test depends on the experience and competence of the user. Home tests have been significantly more accurate when used by older patients or those with higher incomes. The false-negative rate when used at a family planning clinic is lower (16.7%) than when used in a private office (21.1%) or a general public clinic (40.0%).

Monoclonal antibody testing now available for home and office will assist in earlier diagnosis. To improve accuracy, unless medically imperative, patients should be encouraged to wait longer than the six to nine days after the missed menstrual period that manufacturers recommend. Patients must be instructed in the proper technique, including the use of a morning's first urine. When used appropriately, home pregnancy tests enable patients to take increased responsibility for their own health care and minimize potential risks, such as exposure to drugs or irradiation during early pregnancy.

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Immunization Update

MANY REVISED RECOMMENDATIONS for routine immunizations for children, adults, and certain high-risk groups have been published recently. For example, there are now new immunizations for children, and the schedule for routine immunizations has changed. The recent measles epidemic stimulated new recommendations for immunizing adults against measles. There are also new recommendations for certain high-risk groups, such as health care workers and patients with human immunodeficiency virus (HIV) infection.

Children

Originally the *Haemophilus influenzae* type b (Hib) vaccine was recommended for high-risk children at 18 months and all other children at 2 years of age. One *H influenzae* b conjugate vaccine (HibTITER, Lederle) is now available. This new immunization should be given at the 2-, 4-, and 6-month visits (with the oral attenuated poliovirus vaccine [OPV] and diphtheria and tetanus toxoids with pertussis vaccine [DTP]) with a booster at 15 months. Prophylactic acetaminophen administration decreases the systemic side effects of the DTP immunization in children. Other conjugated vaccines may soon be shown to be safe and effective for administration before 15 months of age. Measles immunization continues to be given in combination with mumps and rubella (MMR). Until recently they were given only at 15 months, but now they are given at both 15 months and 4 to 6 years. In areas of high risk, the MMR-1 should be given at 12 months of age. Finally, the 6-month dose of OPV can now be dropped in low-risk areas.

Adults

The influenza vaccine continues as a standard of medical practice to be considered for those with severe medical conditions (especially heart and lung disease), those older than 65, nursing home residents, immunocompromised patients (including people with the acquired immunodeficiency syndrome), and health care workers. All adults older than 65 years and patients with certain chronic medical conditions should receive the pneumococcal vaccine one time. Recent reports that at least 40% of persons 60 years of age and older are not adequately immunized against diphtheria and tetanus should lead to an increased use of the dT immunization.

Special Groups

Three groups deserve special attention. First, all health care providers, especially if they come in contact with bodily fluids, should consider the three-part immunization against hepatitis B. Travelers should contact a local traveler's clinic or the health department at least two months in advance to learn which immunizations are required and recommended for their trip. Finally, those with HIV infection should be up-to-date with their immunizations, especially dT and pneumococcal and possibly measles and influenza. Avoid the OPV vaccine in these immunocompromised patients; the trivalent enhanced-potency, inactivated poliovirus vaccine (IPV) is recommended instead.

A new system was started last year for physicians to report adverse reactions to vaccines. Further information on the Vaccine Adverse Event Reporting System (VAERS) is available 24 hours a day at 1-800-822-7967.

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Intrauterine Devices and Pelvic Inflammatory Disease—A Reanalysis of the Literature

INTRAUTERINE DEVICES (IUDs) are used less and less as a form of contraception in America. This is probably because of decreased marketing due to the litigation related to the Dalkon Shield. Additional concerns with IUDs include side effects of discomfort, increased bleeding, and the traditional belief that IUDs contribute to an increased incidence of pelvic inflammatory disease. There are two IUDs currently available in the United States. The Progestasert must be replaced every year and has a higher rate of ectopic pregnancy than other IUDs. The ParaGard (copper T 380A), a copper IUD, has a failure rate of about 3% and can be left in place for four years at a time.

All IUDs have an increased risk of pelvic inflammatory disease in the first 30 days. This is probably because of contamination of the uterine cavity during insertion. Other causes may include that the tail of the IUD allows bacteria to rise up the cervix and that the IUD will cause local inflammation in the area where it rests. For years, however, a belief has prevailed that IUD use leads to an increased risk of pelvic inflammatory disease after the first 30 days as well. This belief has recently been called into question. In cohort or prospective studies of women with IUDs, the risk of pelvic inflammatory disease was similar to that in sexually active women in industrial countries—about 1% to 2% in the 1970s. In a review of 17 case-control studies, it was found that these studies had often not corrected for oral contraceptive pill use in controls—that is, contraceptive pill use in controls may have provided protection from pelvic inflammatory disease.